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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,169	12/06/2000	Daniel R. Henderson	348022000201	6741

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Linda R. Judge
CELL GENESYS Inc.
342 Lakeside Drive
Foster City, CA 94404

EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1633	9

DATE MAILED: 01/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/732,169	Applicant(s) HENDERSON ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 55-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 55-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to Brian Whiteman, Art Unit 1635.

Non-Final Rejection

Priority

Priority set forth in paper no. 6 filed on 12/6/00 page 2 is acknowledged.

Claims 9-54 have been cancelled and the addition of claims 55-76 in paper no. 6 filed on 12/15/01 is acknowledged.

Information Disclosure Statement

The WO documents and US patents were considered, however the journal articles with the IDS filed with application 09/151,376 have been inadvertently lost. Any publications not initialed have not been considered. Applicants may file copies of these references when filing a new IDS because the examiner has crossed through the references because the information disclosure statement filed on January 16, 2002 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite the journal article(s) listed on the 1449. The title of each journal article is missing.

Note: Applicants should review IDS filed on 1/16/02 because some of the US Patent and WO documents filed in the IDS are on the topic of ceramics (e.g. 1-9, 11-13, 15-16, 19-21, 24, 26, 27, 29, and 37) and do not appear related to the instant application. Therefore, they may have been cited in error.

References that were available have been considered by the examiner, but in order to have the journal articles initialed and dated on the 1449, a new 1449 properly citing the journal articles must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information **not** being considered. See 37 CFR 1.97(i).

Claim Objections

Claims 61 and 68 are objected to for reciting grammatically improper phase, "An cell." Amending the claims to recite 'A cell," would obviate this objection. Claims 61, 68, and 74 are missing a comma after the term E2. Appropriate correction is requested.

Claims 1-8 and 55-76 are pending examination.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time-wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 59, 61, and 67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-8, 28-31, 33-34, 42, and 44-45 of co-pending Application No. 09/151,376. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-6, 8, 59, 61, and 67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1, 3-6, 8-9, and 12 of US Patent No. 5,698,443. For example, claim 5, of patent '443 is drawn to an adenovirus vector comprising at least one of the genes E1A, E1B, or E4 under transcription control of a prostate cell specific response element.

Claims 1-5, 7-8, 59, 61-62, 64-69, and 71-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable as that of claims 1-5, 12-14, 21-23, and 27-32 of U.S. Patent No. 5,871,726. The claims 1-4, 12-13, 21-23, and 27-32 of patent '726 are drawn to an adenovirus vector comprising an adenovirus gene essential for propagation under transcriptional control of a prostate specific response element, said prostate cell specific response element comprising an enhancer specific for prostate specific for prostate specific antigen and a promoter or the adenovirus described above further comprising a transgene, wherein the transgene under transcriptional control of a prostate specific response element (column 41 and 42, claims 1-3). In addition, the claims of the patent are drawn to an in vitro cell comprising either vector described above (column 43, claims 12-14). Furthermore, the claims of the patent are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32). The claims 21-23, and 27-32 of patent '726 are drawn to a method of propagating either adenovirus vector described above into a tumor cell (column 43, claims 21-22) or a method of suppressing tumor growth comprising introducing the either adenovirus vector described above into a tumor cell (column 44, claims 27-32).

Although the conflicting claims in the instant application and patent '726, are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patent uses the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '726 is that the application encompasses the adenovirus vector that is used in the methods of patent '726. Therefore, the claims of the instant application and patent '726 are obvious variants of one another.

Claims 1-5, 7, 59, 61, 64, 67-68, and 71-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of U.S. Patent No. 6, 197,293. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1-6, 12, 14-16, 18, 20, 23-27, 30, 32, and 37-38 of patent '293 are drawn to a replication competent adenovirus vector comprising an adenovirus gene under transcriptional control of a probasin transcriptional regulatory element (PB-TRE), wherein the adenoviral gene is essential for replication (claims 1-6 and 23-26) and a host cell comprising the adenovirus vector (claim 16). In addition, the claims of the patent are drawn to the vector described above further comprising a heterologous gene under transcriptional control of PB-TRE (claims 15, 37-38). The claims 14, 18, 30, and 32 of patent '293 are drawn to a method for propagating the vector in cells (claims 18 and 30). The claims of the patent are also drawn to a method of suppressing tumor growth by contacting tumor cells the vector (claims 20 and 32).

Although the conflicting claims in the instant application and patent '293, are not identical, they are not patentably distinct from each other because each invention encompasses

the same material and the patents use the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '293 is that the application encompasses the adenovirus vector that is used in the methods of patent '293. Therefore, the claims of the instant application and patent '293 are obvious variants of one another.

Claims 1-5, 56-59, 61-66, and 68-73 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-6, 11, and 37 of US Patent No. 6,254,862. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims 1, 3-6, 11, and 37 of patent '862 are drawn to a replication competent adenovirus vector comprising E1A and E1B wherein E1A and E1B are both under transcriptional control of separate alpha fetoprotein transcription elements (AFP-TRE), wherein at least one AFT TRE comprises either an enhancer or a promoter from an AFP gene (claims 1, 3-6) and a host cell comprising the vector described above (claim 11). In addition, the claims of the patent are drawn to a method of suppressing tumor growth in an individual be contacting a tumor cell with the adenovirus vector (claim 37).

Although the conflicting claims in the instant application and patent '862 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the adenovirus vector encompassed in the instant application. The difference between the claims of the instant application and patent '862 is that the adenovirus is patent '862 is a replication competent adenovirus vector comprising two

adenoviral genes, which are both under control of an AFP-TRE. Therefore, the claims of the instant application and patent '862 are obvious variants of one another.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2-5 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The statement in claims 2-5 and 8, "**An** adenovirus of claim ..." is indefinite because it does not point out which composition **an** adenovirus is referring to in the claim. The dependent claim should state "The adenovirus of claim."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 and 55-76 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure, which is not enabling. A replication competent adenovirus vector is considered critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The claimed invention encompasses a replicant competent adenovirus vector and the specification as a whole only teaches the concept of making and/or using "a replication competent adenovirus vector" (page 5, line 14). It appears from the specification that the only adenovirus vector contemplated by the claimed invention is the replicant competent adenovirus, however the

claims do not include the essential material. In view of *In re Mayhew*, the claims are not enabled by the disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-6, 8, and 55-76 are rejected under 35 U.S.C. 102(e) as being anticipated by Gregory et al. (US20001/0053768, filing date 5/3/95). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen promoter/enhancer, the prostate specific antigen promoter/enhancer, or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 7, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1 genes, E2 gene, or E4 gene (page 7, claims 16-18).

Claims in the instant application (e.g. 1-3, 5-6, 55) read on either a replicant competent or a replicant defective adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific TRE. Therefore the following rejection under 102(b) follows since the claims read on a replicant defective adenovirus vector.

Claim 1-3, 5-6 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Friedman et al. (Transcriptional Control Mechanism, pp 421-435, 1987). Friedman replaced the normal regulatory element found at the left end of the adenovirus genome (e.g. E1A) with a tissue specific promoter (e.g. albumin) (page 425). In addition, Friedman teaches that the Ad vector with the tissue specific promoter directed the synthesis of E1B gene and the expression of the early viral E2a and E4 genes (pages 426-427).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, and 55-76 are rejected under 35 U.S.C. 103(a) as being unpatentable by Gregory et al. (US20001/0053768, filing date 5/3/95) taken with Bohinski et al. (Mol Cell Biol, Vol. 14, 1993, abstract), Abe *et al.* (PNAS, Vol. 90, 1993, abstract), Grooteclaes et al., (Cancer Res., Vol. 54, abstract, 1994). Gregory teaches a method of treating mammalian cancer cells, comprising administering a replication competent adenoviral vector comprising a therapeutic gene and a disease specific gene regulatory region operationally linked to at least one replication gene wherein the cancer cells activate the tumor specific gene regulatory region causing the adenoviral to replicate (page 7, claim 1). Furthermore, Gregory teaches using the alpha-fetoprotein promoter/enhancer, the carcinoembryonic antigen (CEA) promoter/enhancer, the prostate specific antigen promoter/enhancer, or the tyrosinase promoter/enhancer (page 7, claims 2, 4, 7, 9, respectively). Gregory further teaches that the replication gene used for making the vector in the method described above is a viral E1 genes, E2 gene, or E4 gene (page 7, claims 16-18). Gregory does not an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE.

Regarding claims drawn to specific TREs, Abe, Grooteclaes, and Bohinski teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made.

It would have been obvious for one of ordinary skill in the art to have modified the adenovirus vector taught by combining Gregory with taken with Bohinski, Abe, Grooteclaes, to produce an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a DF3-TRE, a surfactant TRE, and an ErbB2-TRE. It would also have been obvious for one of ordinary skill in the art to have constructed and employed the tissue-specific-replication competent adenoviral vectors by using a known tissue-specific promoter operably linked to a viral gene necessary for adenoviral replication for expressing a cytotoxic gene in a tumor cell-specific fashion in order to target and deliver the cytotoxic gene product to tumor cells. One of ordinary skill in the art would have a reasonable expectation of success in constructing and employing the tissue-specific-replication competent adenoviral vectors, particularly since Abe, Grooteclaes, and Bohinski all teach that tissue-specific promoters including DF3, surfactant, and ErbB2 are known in the art at the time the invention was made and employed for delivery of gene products to targeted cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-7, 55-56, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCormick (US Patent No. 5,667,178, filing date 2/16/94) taken with Glazenburg et al. (WO 92/03563), Berkner et al. (Biotechniques, Vol. 6, 1988, pp. 616-629), Roth *et al.* (US Pat No.

5,747,469). McCormick infects neoplastic cells and non-neoplastic cells with a wild type adenovirus and shows that the wild type virus kills both types of cells (column 19, lines 10-column 20-line 23). However, McCormick does not teach an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE).

However, at the time the invention was made, Glazenburg teaches using a microorganism (e.g. virus) brought under control of nucleotide specific for the cell, the tissue or the host, and wherein at least one essential gene of the virus has been brought under control of a nucleotide sequence specific for the cell, the tissue, or the host and using the microorganism to combat tumors (page 8, lines 4-11 and page 11, line 1-10, lines 33-34). Furthermore, Glazenburg teaches that the virus does not differ from the wild-type virus (page 7, lines 15-25). Glazenburg further teaches that another advantages arises in the case of using a promoter/enhancer which is expressed only in specific cells because the virus will only destroy the harmful cells and leave healthy cells unharmed (page 7, lines 15-25 and lines 31-37).

Roth teaches a method for killing tumor cells *in vivo* wherein any recombinant adenovirus available in the prior art of record encoding a tumor suppressor gene is employed (abstract, claims 2, 15, 105). Roth teaches that an adenovirus system has potential advantages for gene delivery *in vivo,* such as ease of producing high titer virus, high infection efficiency, and infectivity of many types of cells (column 2 bridging column 3). Column 7, lines 28-30 specifically disclose that, "other than the requirement that the adenovirus vectors be engineered to express p53, the nature of the initial adenovirus is not believed to be crucial to the successful practice of the invention." In addition, Berkner teaches a number of advantages (i.e., broad host

specificity, and the prompt onset of transcription and translation following infection of the vectors allows analysis that is less dependent upon mRNA and using Ad vectors for tissue-specific expression of any recombinant adenovirus vector.

One of ordinary skill in the art would have been motivated to have further modified the adenovirus of McCormick by incorporating a TRE in the adenovirus so as to regulate expression of any adenovirus essential gene thereby rendering tissue specific for the intended activity of the adenovirus because Glazenburg teaches that by employing a tissue specific TRE to drive expression of an essential viral gene in a replication competent virus used in the treatment of tumors, only intended target neoplastic cells of the tumors from the tissue for which it has been rendered specific will be combated by the virus, and thereby leaving the normal or non-specific cells unharmed, and because Berkner teaches a number of advantages of using an adenovirus having a tissue specific promoter operably linked an adenoviral essential gene, wherein the advantages include: broad host specificity, and the prompt onset of transcription and translation following infection of the vectors allows analysis that is less dependent upon mRNA and protein stability than transfection experiments. Note that Roth also teaches that, other than the requirement that the adenovirus vectors be engineered to express p53, the nature of the initial adenovirus is not believed to be crucial to the successful practice of the invention." As a result, one of ordinary skill in the art would have a reasonable expectation of success to construct and use the replication competent adenovirus of the combined cited references as a whole for the purpose of only targeting neoplastic cells to combat tumors located in an intended target tissue, particularly since both McComick and Roth all teach and demonstrate that any recombinant adenovirus can be used to kill tumor cells.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-8 and 55-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCormick (US Patent No. 5,667,178, filing date 2/16/94) taken with Glazenburg et al. (WO 92/03563), Berkner et al. (Biotechniques, Vol. 6, 1988, pp. 616-629), and Roth *et al.* (US Pat No. 5,747,469) in further view of Bohinski et al. (Mol Cell Biol, Vol. 14, 1994, abstract), Abe *et al.* (PNAS, 90: 252-286, 1993), Grooteclaes *et al.,* (Cancer Res., 54: 4193-4199, 1994), Richards et al., (WO95/14100), Vile et al. (Cancer Res., Vol. 53, abstract, 1993), Riegman et al. (Mol Endocrinol., 1991, Vol. 5: abstract, 1991) and Watanabe et al. (J. Biol. Chem. 262, abstract, 1987).

The rejections of the base claim 1-3 and 56 under 35 U.S.C. 103(a) are applied here as indicated above, e.g., McCormick taken with Berkner, Roth, and Glazenburg. McCormick taken with Berkner, Roth, and Glazenburg do not an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a prostate cell specific, an alpha-fetoprotein TRE, a DF3-TRE, a tyrosinase-TRE, a CEA-TRE, a surfactant TRE, and an ErbB2-TRE and a cell or producer comprising the adenovirus vector described above.

Regarding claims drawn to specific TREs, Bohinski, Abe, Grooteclaes, Richards, Vile, and Watanabe teach that tissue-specific promoters: prostate cell specific, alpha-fetoprotein TRE, a DF3-TRE, a tyrosinase-TRE, a CEA-TRE, a surfactant TRE, and an ErbB2-TRE are known in the art at the time the invention was made.

It would have been obvious for one of ordinary skill in the art to have modified the

adenovirus vector taught by combining Gregory with taken with Riegman, Bohinski, Abe, Grooteclaes, Richards, Vile, and Watanabe, to produce an adenovirus vector comprising an adenovirus gene under transcriptional control of a cell type specific transcriptional response element (TRE), wherein the TRE is selected from the group consisting of a prostate-TRE, a DF3-TRE, a surfactant TRE, and an ErbB2-TRE. It would also have been obvious for one of ordinary skill in the art to have constructed and employed the tissue-specific-replication competent adenoviral vectors by using a known tissue-specific promoter operably linked to a viral gene necessary for adenoviral replication for expressing a cytotoxic gene in a tumor cell-specific fashion in order to target and deliver the cytotoxic gene product to tumor cells. One of ordinary skill in the art would have a reasonable expectation of success in constructing and employing the tissue-specific-replication competent adenoviral vectors, particularly since Riegman, Bohinski, Abe, Grooteclaes, Richards, Vile, and Watanabe teach that tissue-specific promoters: prostate, alpha-fetoprotein TRE, a DF3-TRE, a tyrosinase-TRE, a CEA-TRE, a surfactant TRE, and an ErbB2-TRE are known in the art at the time the invention was made and employed for delivery of gene products to targeted cells.

Furthermore, it would have been obvious for one of ordinary skill in the art to make a producer cell comprising the vectors described above. One of ordinary skill in the art would have been motivated to use a producer cell because of the routine practice of increasing a titer of a virus comprising an adenovirus vector by using a producer cell line.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

Brian Whiteman
Patent Examiner, Group 1635
January 25, 2001